EXHIBIT 2

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

IN RE: Bair Hugger Forced Air Warming Products Liability Litigation	Case No. 0:16-cv-04159 (JNE/DTS)
This Document Relates to All Actions. **PLAINTIFF(S)** **ADA TROMBLEY** **VS.** **3M COMPANY,** **a Delaware Corporation**	**PLAINTIFF'S EXPERT REPORT**

January 25, 2019

Plaintiff herewith submits the expert report of William R. Jarvis, M.D.

Jason and Jarvis Associates, LLC

January 25, 2019

I. INTRODUCTION

This specific causation expert report concerns the periprosthetic joint infection (PJI) suffered by Mrs. Ada L. Trombley ("Mrs. Trombley"). I hereby reincorporate, in its entirety, my expert report previously provided with respect to general causation, including citations and exhibits, as if fully stated here. I also re-incorporate my deposition testimony and opinions previously provided with respect to general causation.[1]

In addition to the documents I reviewed previously for my general causation expert report, I have also reviewed Mrs. Trombley's medical records, along with the deposition transcripts of Certified Registered Nurse Anesthetist (CRNA) Peterson, Orthopedic Surgeon Dr. Beer, and Anesthesiologist Dr. Abdul-Aziz. (See Exhibit A). If additional discovery is taken and depositions conducted, I reserve the right to review those depositions as well and to comment on any opinions expressed therein. In addition, there may be documents produced by Defendants and/or third parties in this matter that may impact my opinions as well. I therefore reserve the right to amend and/or supplement this report upon receipt and review of additional information obtained through such discovery, to include expert witness discovery. Finally, if there is any further information provided concerning the ProMedica Hospitals HVAC system used in O/R number 3 on the date in question, whether documentary or in the form of deposition testimony, I would like the opportunity to review and determine what, if any impact, such discovery may have on my opinions in this matter.

II. BRIEF MEDICAL HISTORY OF MRS. TROMBLEY

Based on my careful review of the records in this case, and my experience as a medical doctor and a clinician, it is my opinion to a reasonable degree of medical certainty that Mrs. Trombley was an appropriate candidate for her right total knee arthroplasty (TKA) surgery and that the pre-operative skin preparation,

[1] Given recent developments in the published, peer-reviewed literature, I expressly request the right to supplement my general causation expert report in the MDL for purposes of up-dating my opinions based on new information and data.

antibiotic/antimicrobial prophylaxis, and incision care that were employed throughout the surgery complied with the standard of care.

Mrs. Trombley was a 62-year-old female with a long history of osteoarthritis of her knees (she had a previous left TKA in August 2001), type-2 diabetes mellitus, hypertension, obesity, gastrointestinal reflux (GERD) and "psoriatic arthritis" for which she took 10 mg of Prednisone daily. Mrs. Trombley underwent a right TKA on December 2, 2011. Mrs. Trombley was 5 feet 3 inches (162 cms) tall and weighed 212 pounds (96 kgs), giving her a body mass index [BMI] of 36. She did not have a history of smoking or alcohol use. After the failure of conservative therapy for her right knee pain, she was scheduled for a right TKA. An x-ray of her right knee showed "severe medial compartment osteoarthritis." Mrs. Trombley had a pre-operative evaluation by an internist for surgical clearance. She was cleared for surgery, and no concerns were raised about her dentition, creatinine or genitourinary tract.

On December 2, 2011, she underwent a right TKA performed by Dr. Karl Beer at ProMedica Bay Park Community Hospital, Oregon, Ohio. Pre-operatively at home she was told to bathe the morning of surgery with Hibiclens (i.e., Chlorhexidine or CHG); the pre-operative checklist indicates this was done. She was given "CHG soap instructions" on how to bathe with CHG at home. After hospital arrival and before her right TKA, she was again bathed with a CHG cloth. At the time of her surgery, her American Society of Anesthesiologists (ASA) score was 3, her blood sugars were 81-140 mg/dl, her blood pressure was 166/77, and her creatinine was 1.2 mg/dl. Mrs. Trombley was not intubated; she received spinal (rather than general) anesthesia. Her pre-operative skin preparation was Chloraprep (from thigh to toes and with a three minute dry time). She received 2 grams of Ancef as a prophylactic antimicrobial at 9:09 am on December 2, 2011 (i.e., 21 minutes before the incision at 9:30am). Medical records confirm a Bair Hugger blanket was placed on Mrs. Trombley and used throughout her right TKA surgery (Bair Hugger #11534). The right knee tourniquet did not work properly and after two attempts to get it to work, it was removed and no tourniquet was used during this procedure (so blood with antibiotic perfused her knee during the entire procedure). Records further confirm that Mrs. Trombley' body temperatures intra-operatively were: 36^{o}C, 36^{o}C, 36^{o}C, 37^{o}C, 37^{o}C, and 37^{o}C.

The time of surgery was 71 minutes (9:30 am-10:41 am). Mrs. Trombley's surgery was performed in Operating Room (OR) 3 at Bay Park Community Hospital and seven personnel participated in the surgical procedure. Her implants included: Vanguard or femoral right interlock (Biomet), fixed I-beam tibial plate with locking bar (Biomet), series a standard patella (Biomet), cobalt HV with gentamicin (Biomet), and Vanguard DOM tibial bearing anterior stabilized (Biomet). No drains

were inserted. Mrs. Trombley had a Foley catheter inserted pre-operatively which was discontinued on December 4, 2011. Mrs. Trombley's estimated blood loss was 400 ml (anesthesia) or 150 ml (post-operative procedure report by Dr. Beer) and urine output was 200 ml. Before closure, the surgical site was irrigated with saline plus Betadine. Mrs. Trombley had an x-ray of her right knee on post-operatively on December 2, 2011, which showed "no acute fracture," "joint replacement looks anatomic," "skin staples and postoperative gas noted."

Mrs. Trombley's post-operative course was unremarkable. Post-operatively, Dr. Beer consulted with Charles Sheldon, D.O. to assist with her medical care. Her post-operative laboratory values included: a white blood count (WBC) of 15,100 to 16,800 cells/mm^3; glucose of 68-140 mg/dl; creatinine of 1.17-1.21 mg/dl; and HGB A1C of 5.4 (normal 4.2-5.8). Mrs. Trombley received one gram of Ancef every eight hours for two doses post-operatively. Importantly, during her admission, there were no abnormalities or concerns mentioned about her Ear, Eyes, Nose and Throat (EENT), gastrointestinal or genitourinary tracts, or skin. On December 4, 2011, Dr. Beer discharged Mrs. Trombley to her home and stated that she was "doing well" and "wound healing well."

Next, Mrs. Trombley was seen in Dr. Beer's office on December 15, 2011 for her two-week check-up and staple removal. At that time, she had "improving pain and swelling, but no abnormal bleeding." The surgical incision was reported as "clean, dry and intact" with "ecchymosis from lower leg and calf to mid thigh and swelling (localized hematoma; medial tibial condyle), but no warmth, induration and no erythema." Dr. Beer concluded that Mrs. Trombley was "progressing slowly, but with good pain control and without signs of an infection." There was no evidence of any superficial surgical wound infection (SWI).

Mrs. Trombley returned to Dr. Beer's office on January 10, 2012 with complaints of drainage from her knee for four days, fever, chills and increasing pain. On examination, she was found to have serous and purulent drainage "<2 cm wound to proximal end of the incision." The right knee was swollen, but had "no erythema, ecchymosis or tenderness." He attempted an aspiration of the wound in his office which was unsuccessful (i.e., no fluid obtained). Thus, Mrs. Trombley had no physical signs of a superficial wound infection, commonly referred to as a superficial SSI, and the failure to aspirate any pus suggests that the infection was deep, involving the joint and implant. Mrs. Trombley had a WBC of 20,000 (66% segs and 1% bands), a C-reactive protein (CRP; normal 0-0.744) of 12.5 and an Erythrocyte Sedimentation Rate (ESR; normal 0-30) of 52. Dr. Beer concluded that she had a "seeping wound" and "possible infection." A swab of the wound showed 0-1 WBCs and many Gram-positive cocci on Gram's stain and subsequently grew Group B Streptococcus (GBS). Because of her potential infection, Dr. Beer

admitted Mrs. Trombley to the Toledo Hospital for "an incision and drainage (I&D) and placement of a wound vac." At no time was there any comment or reference to a hematoma, or any suggestion at all that this deep joint infection was being treated as a superficial SSI.

On January 11, 2012, Mrs. Trombley was taken to the OR for an "infected right total knee." Dr. Beer noted that she had "gross purulence from the mid upper portion of her knee incision" and "the opening was found to be a large cavity full of purulent material" and that "it was felt the implant was involved." The surgical site was opened, the joint entered, and multiple cultures were obtained. After the cultures were obtained, she received intravenous Daptomycin. Because of involvement of the prosthesis, Dr. Beer decided to remove all the implants and cement, perform a complete synovectomy, and copiously irrigate the surgical wound with four liters of "antibiotic saline." In addition, 65 femoral and 65 tibial cement spacers were made and inserted. Two units of cobalt G was mixed with 6 grams of vancomycin and 4.8 grams of tobramycin and injected into the femoral mold. A third unit of cement with 3 grams of vancomycin and 3.6 gms of tobramycin tibial mold was made. In addition, a unit of cement with 3 grams of vancomycin and 3.6 grams of tobramycin were made.

Cultures obtained on the January 11, 2012 right TKA I&D and implant removal surgery included:

Deep wound: Gram stain: 0 WBC and no organisms seen; culture: rare GBS.

Wound swab (anaerobic): Culture: rare GBS; no anaerobes.

Right knee synovium: Gram stain: 10-20 WBC and no organisms seen; Culture: few GBS.

Right knee synovium (anaerobic culture): rare GBS.

During this January 11, 2012 admission, Mrs. Trombley had a WBC of 13,700 cells/mm3, glucoses of 52-179 mg/dl, Creatinines of 0.95-1.06, a HGB A1C of 5.5, and was found to be nasal methicillin-resistant S*taphylococcus aureus* (MRSA) polymerase chain reaction (PCR) negative. Postoperatively, Mrs. Trombley was seen by an infectious diseases physician, Nelson Nicolasora, M.D., who recommended a six-week course of Ceftriaxone (completed on February 28, 2012, at which time her peripherally inserted central catheter [PICC] was removed) and she was continued on suppressive Cefelexin orally (subsequently discontinued on September 13, 2012, when Augmentin was started orally). Mrs. Trombley's serial CRPs and ESRs remained elevated from January 12, 2012 until April 16, 2012.

During Mrs. Trombley's antimicrobial therapy, her creatinine increased from 1.03 on January 21, 2012 to 2.75 mg/dl on April 16, 2012 (and remained in the 2.19 to 2.75 range from April 16, 2012 to March 18, 2016). Because of this elevating creatinine, Mrs. Trombley was referred to a nephrologist, Nina Al-Sabbagh, M.D., for evaluation on March 26, 2012. At that time, an ultrasound of her kidneys was normal with no evidence of hydronephrosis. On May 17-18, 2012, a serum protein electrophoresis and immunoglobulin levels were normal, her WBC was 8,200 cell/mm^3, an immune work-up was negative (ANA, ANCA, etc.). On May 3, 2012, a urine culture was negative showing no evidence of a urinary tract infection. She was followed by Dr. Al-Sabbagh until September 17, 2012. Mrs. Trombley's creatinine remained "relatively stable" and no specific etiology of her post-operative "acute on chronic renal failure" was ever indicated in the medical records from the nephrologist.

On August 31, 2012, Mrs. Trombley underwent the second surgery of the two-stage revision to her right knee: the re-implantation. After confirming that the previously-documented right TKA infection was resolved and her CRP and ESR were normal, the right TKA re-implantation proceeded. Many of the elements in this surgery were similar to the previous two right knee surgeries (i.e., ASA, BMI, no endotracheal intubation, spinal anesthesia rather than general anesthesia, pre-operative skin preparation with Chloraprep, no use of a right knee tourniquet, and use of an upper body Bair Hugger blanket throughout the procedure). At the time of her re-implantation surgery, there was "no evidence of any acute inflammation" of her right knee area and "the bone was healthy." The cement used for implant was mixed with Ancef, and the wound was irrigated with Betadine before closure.

Conclusion and Synopsis of Key Opinions

All the opinions I express in this report are opinions I hold to a reasonable degree of scientific and medical probability.

On December 2, 2011, Mrs. Trombley underwent a right TKA procedure (i.e., index procedure). Her pre-operative skin preparation (i.e., home hibiclense bathing, pre-operative CHG cloth bathing, and then skin antisepsis with Chloraprep) and prophylactic antimicrobial agent, dose, and timing (i.e., 2 grams of Ancef administered intravenously 21 minutes before incision) were consistent with applicable guideline recommendations and followed appropriate standards of medical practice at all times. The duration of the initial right TKA implant surgery was 71 minutes. Regional spinal anesthesia without endotracheal intubation was given. The estimated blood loss was 150-400 (surgeon vs anesthesia personnel) and no red blood cell transfusions were given. I am unaware of any reports of

contaminated surgical tools or supplies, nor any deviations from standard surgical practice or infection control procedures. Based on my review of available records, the medical care comported with all accepted standards of medical and surgical practice.

Despite the appropriate care provided by the medical care professionals, approximately 39 days after the index procedure, Mrs. Trombley was diagnosed with a prosthetic joint infection (PJI) which necessitated a two-stage revision surgery including removal of her right TKA prosthesis, and placement of antibiotic spacers followed by six weeks of intravenous and then oral prolonged suppressive antimicrobial therapy with agents targeting Gram-positive cocci, including GBS. After the infection cleared, a permanent knee prosthesis was re-implanted. The findings of right knee clinical signs/symptoms (i.e., swelling with chills, fever and purulent drainage); elevated WBC, ESR, and CRP; growth of GBS from multiple cultures (including deep swabs, intra-operative cultures of the wound and synovium), and visual evidence of a PJI at the time of the implant removal surgery, along with Mrs. Trombley's response to antimicrobial therapy (six weeks of Ceftriaxone and then suppressive Ancef), are all consistent with a nosocomial, including the Centers for Disease Control (CDC) or Surgical Infection Society (SIS) definitions, of a PJI.

III. METHODOLOGY

Health care providers routinely use a causation assessment that courts sometimes refer to as a "differential diagnosis" or "differential etiology" in assessing the underlying cause of a patient's medical condition. This methodology requires "ruling in" all potential causes of the condition and then "ruling out" unlikely causes of the condition. Here, this generally accepted methodology requires that I rule in all potential causes of the bacteria inoculating the joint, and then ruling out unlikely causes of the bacteria that inoculated the joint based on the facts and evidence presented. As to biological plausibility, pathogens are the actual ***causes*** of the PJI; that is, the only biological causes of infection in the orthopedic implant arena are bacteria that have inoculated the joint. The general consensus is that PJI's that occur within 90 days and in some instances up to one year after the index surgery are most likely caused by inoculation of the joint during the surgery.

Using the foregoing method to identify potential causes of Mrs. Trombley's PJI, medical literature confirms that the majority of PJIs are caused by pathogens that are deposited in the surgical wound during the surgery.[2] Put simply, without microbial

[2] *See* Jarvis General Causation Expert Rpt. at 4–8, 16 (collecting scientific sources).

pathogens and dissemination to the deep joint space, ***no patient*** would suffer PJI regardless of how many risk factors he or she may possess or his or her susceptibility to infection.[3] Notably, while speculating that she may have been infected after she left the hospital, even Dr. Beer, her treating orthopedic surgeon, agreed with this concept. (Beer Depo at p:98; ll:1-8; p:109; ll:14-24) While it is true that Mrs. Trombley—like nearly all TKA patients—had several risk factors that might tend to increase her susceptibility to infection if and when exposed to pathogens, (e.g., obesity and type-2 diabetes), it is my clinical and professional medical opinion that none of these conditions impacted her actual ***development*** of PJI. For example, medical records confirm that Mrs. Trombley's blood sugar levels were below 150 mg/dl before, during, and after surgery; her dosage of prednisone would not be immunosuppressive; she had no previous history of GBS infections at any site; and there was no evidence of dental infection at the time of her index right TKA.

Based on my review of the medical records in this case, my differential diagnosis/etiology confirms that the care rendered to Mrs. Trombley, the practices of the surgical team, and other applicable factors, together with the medical literature concerning forced air warming (FAW) technology and Bair Hugger warming specifically, and the mechanistic Computational Fluid Dynamics (CFD) study performed by Dr. Elghobashi in other cases, the most likely source of Mrs. Trombley's PJI was the inoculation of her surgical wound with GBS at the time of her index surgery.

Relevant medical literature confirms that the vast majority of bacteria, often measured as colony forming units ("CFUs"), in the OR come from the surgical team.[4] Knowing the overwhelming majority of PJIs are caused by bacteria deposited during surgery, I turn to the potential sources of pathogens inside the OR.

A. Rule In / Rule Out: Potential Causes of Bacteria Contaminating the Joint

1. Bair Hugger

The Bair Hugger significantly increases the quantity of particles and thus bacteria over the sterile surgical field resulting in a significantly increased risk of PJIs as previously outlined in my general causation expert report and deposition. *It is my expert opinion to a reasonable degree of medical probability that when a Bair*

[3] As discussed during my deposition, these "risk factors" do not ***cause*** PJI but rather may increase the likelihood that PJI ***will develop if*** bacterial contamination of the prosthesis/joint/incision occurs. Indeed, offending pathogens or CFUs must not only exist, but such pathogens must deposit at the surgical site in the prosthesis/deep joint space in order for a PJI to occur at the time of surgery.

[4] *See* Jarvis General Causation Expert Rpt. at 5 (citing, *e.g.*, Whyte 1988) *see also id.* at 21 (noting patient-specific interventions that reduce likelihood of patient as cause).

Hugger blanket is used during orthopedic arthroplasty surgeries, it substantially increases the risk of a PJI.

The following points support my opinion that the Bair Hugger significantly increases risk of PJIs:

- As outlined in my expert report on general causation, a thorough review of the peer-reviewed medical literature, including the elevated odds-ratio reported in the McGovern study[5], increased particles over the operative foeld when the Bair Hugger is turm on. and various case reports document the increased risk of SSI associated with Bair Hugger forced air warmers.

- As explained further below, I find persuasive the expert CFD report of Dr. Said Elghobashi regarding the Bair Hugger 750, along with his supplemental report regarding the impact of the Bair Hugger 505, on the OR unidirectional airflow. According to Dr. Elghobashi's study, the Bair Hugger causes significant disruption of OR airflow, leading to increased number of particles and skin squames over and in the sterile field. Dr. Elghobashi's report has been subject to the rigors of peer review, and published in an internationally-renowned journal. Further, the ICOS which met for a second time in 2018, cited Dr. Elghobashi's article and recognized the theoretical risk forced air warming devices play in causing PJI's. (Pakseresht P, Apte SV, Elghobashi S. Effect of heated-air blanket on the dispersion of squames in an operating room. Int J Numer Method Biomed Eng 2018;34:e2960.)

- As further detailed in my general causation report, the Bair Hugger has two mechanisms for contaminating the operative field with bacteria—through blowing non-filtered, non-sterile air and through releasing excess heat that disrupts OR airflow. Each mechanism causes increased particles and skin squames and therefore bacteria over the sterile field.

2. Surgical Team Contamination

The surgical team, if not properly scrubbed in, may contaminate the sterile field and increase the risk of infection, including increasing the risk for PJI during TKA. Records do not show that the surgical team failed to follow the appropriate aseptic procedures and sterile techniques. In fact, Dr. Beer wore a "spacesuit" during Mrs. Trombley's TKA procedure. Absent evidence to the contrary, the surgical team complied with appropriate standards of care, rendering the likelihood

[5] *See* section III(b), *infra.*

of the surgical team's contaminating the wound very small. It is my professional expert opinion that the surgical team did nothing to increase the risk of infection during Mrs. Trombley's surgery and that her infection was not the result of any action or inaction by this team.

3. Patient's Flora

One of the potential sources of bacteria is the patient's flora at or immediately adjacent to the surgical incision. However, there is a general consensus that many if not most PJIs are caused by airborne contamination.[6] The skin squames of surgical personnel or the patient released into the environment can then through turbulent air circulation contaminate the surgical wound or sterile equipment or materials used in the surgical procedure. The use of Chloraprep (i.e., 2% chlorhexidine and 70% isopropyl alcohol)—two highly effective skin antiseptics—as skin preparation would nearly eliminate skin flora at the surgical incision site and therefore the likelihood of the PJI being caused by the patient's own flora around the surgical site is very unlikely. In addition, Mrs. Trombley used Hibiclense to bathe at home the night before her surgery and had a CHG cloth applied immediately before being taken to the OR. Furthermore, GBS is a rare superficial skin colonizer and is an unusual cause of dental caries or periodontal disease. GBS can colonize the gastrointestinal or genitourinary tract, but Mrs. Trombley had no evidence of any gastrointestinal or genitourinary tract issues at the time of her index right TKA surgery (including being evaluated by an internist and cleared for surgery). Subsequently, as a part of Mrs. Trombley's nephrology evaluation, she had a urine culture and it was not positive for GBS. Thus, Mrs. Trombley's own flora can be properly ruled out.

4. Surgical Procedure and Technique

Based on my review of the medical records, together with deposition testimony of treating doctors in this case, it is evident that the surgeons and staff followed appropriate standards of care and proper surgical procedure and technique. There is no evidence that at any time of the procedure there was a break in the sterile field by any procedure or technique documented in the medical records. In fact, the medical records indicate and Dr. Beer confirmed that no adverse events occurred during the operative procedure. There was no evidence of any contamination of the surgical instruments or iatrogenic contamination of the sterile field. Based on the records reviewed, it is my opinion held to a reasonable degree of medical probability that the surgical procedure and technique were within the standard of care and that the likelihood of the surgical procedure or technique of the surgical team causing

[6] *See, e.g.*, PROCEEDINGS OF THE INTERNATIONAL CONSENSUS MEETING ON PERIPROSTHETIC JOINT INFECTION (2013) at 115–16 ("[T]he focus of our recommendation is to reduce the volume of bacteria in the operating room with particular attention to airborne particles.").

bacteria to inoculate the joint is very low. The surgical procedure and technique can therefore be ruled out as a likely cause, within a reasonable degree of medical probability.

5. Other Potential Causes

Based on the testimony of Dr. Beer, Dr. Abdul-Aziz, and the CRNA Peterson, I am even more confident that there are no other likely, potential causes of bacteria reaching the sterile field during Mrs. Trombley's surgery. For example, I saw no evidence that the HVAC system in question may have been deficient in any respect or contributed in any way to this infection. I reviewed the HVAC system operating manual, and it shows unequivocally that the air exchange rates were well in excess of what ASHRAE standards prescribe (20 exchanges/hour); furthermore, the surgery was conducted in a new and modern OR, with positive downward airflow and multiple levels of filtration. Without some kind of affirmative evidence to suggest the system did not perform as designed, there is no plausible basis to suggest the HVAC system contributed to Mrs. Trombley's infection. Thus, based on the HVAC documents reviewed, together with the medical records, the medical testimony, my experience, and the published peer-reviewed scientific literature, I have compiled the list above regarding potential causes of bacteria reaching the sterile field. I reserve the right to supplement this section and report if any new information should arise from any additional depositions of fact witnesses or other discovery regarding this matter, including discovery of hospital personnel.

6. Possible Causes Ruled Out

I have considered the following possible causes and have not ruled them in as plausible sources that can cause bacteria to inoculate the joint or other areas of the sterile field: anesthesia machines; surgical lights; computer monitors; computer consoles; electrocautery devices; bovie; surgical drapes; cabinets along the walls; the suction drain; sterilized surgical equipment; drop buckets; trash receptacles; or surgeons moving their hands. Based on my review of the literature, my training, education, and experience, there is no evidence in the scientific community indicating that any of the foregoing variables increase the likelihood of bacteria inoculating the joint. Nor do any of the medical providers in this case identify any such other equipment as being potentially causative of the infection in this case. (See generally, depositions of Dr. Abdul-Aziz, Dr. Beer, and CRNA Peterson.) Furthermore, Mrs. Trombley had no evidence of active infection at any site (as evidence by her medical clearance), including the gastrointestinal, genitourinary, or oral/dental sites. Any suggestion that her poor dentition may have been somehow related to her developing a deep joint infection in her knee is pure speculation and utterly without foundation. Poor dentition has never been found to be a risk factor for GBS infection, particularly a GBS-PJI. As previously mentioned, the fact that on

the two week post-operative check-up Dr. Beer did not see any external signs of superficial SSI and his attempted aspirate in January 2012 did not obtain pus, indicates that this was a deep infection or PJI (as Dr. Beer indicated at the time of the January 2012 surgery in which he removed the prosthesis) and not a superficial SSI that progressed deeper.

B. Bair Hugger is the Most Likely Cause of Bacteria Inoculating the Joint

1. Methodology using Relative Risk and Differential Etiology

Differential diagnosis and/or etiology often use epidemiological studies and relative risk ratios to determine causation in a specific case. As discussed below, numerous studies, including the McGovern study, indicate directly and indirectly that the Bair Hugger more than doubles the risk of PJI. A relative risk ratio equal to or greater than 2.0 indicates that a device or drug is the most likely cause of the disease. Thus, absent any deviation from the standard of care by the physicians, staff, or hospital, the Bair Hugger is the most likely cause of a patient's PJI in an orthopedic arthroplasty surgery.

In the case of Mrs. Trombley, I have analyzed all other plausible causes of a PJI in surgery and have used her medical records to rule out those variables as the most likely cause of her implant being inoculated with bacteria causing his PJI. The McGovern study and/or Dr. Elghobashi's CFD model paired with the Stocks and Darouiche studies each independently confirm that the Bair Hugger is the most likely cause of Mrs. Trombley's PJI.

2. Quantifying the Risk Posed by Bair Hugger

a. CFD Model and Peer-Reviewed Literature

The results of Dr. Elghobashi's CFD test makes clear that the Bair Hugger causes significant turbulence in the OR, particularly around the OR table. As a result of that disruption, the Bair Hugger significantly increases the number of skin squames and particles reaching the surgical site, the OR table, and side tables where instruments, fluids, and implants are located. Indeed, the Bair Hugger increases the density of particles large enough to carry bacterial CFUs by more than 10 CFU/m^3 in a very short time. The International Consensus of Orthopedic Surgeons (ICOS), along with a large body of medical literature, confirms that the probability of PJI correlates directly with the quantity of bacteria that reaches the surgical wound during an orthopedic arthroplasty procedure. The ICOS also recognizes the mechanistic theory advanced by Mrs. Trombley here: that forced air warming devices may cause PJIs. The literature also demonstrates that use of the Bair Hugger increases particles, and thus bacteria, over the sterile field. The overwhelming numbers of particles in the OR are from the surgical staff and patient. A range of at

least 1 million to as much as 900 million skin squames are shed, per hour, by surgical staff during a typical procedure.

As discussed in my general causation report, the Stocks and Darouiche studies correlate particles and CFU over the surgical site. Stocks et al. correlated the number of CFUs with the number of 10 micron particles, while Darouiche et al. correlated the number of CFUs with the incidence of PJI in orthopedic procedures. Based on the empirical data collected in the Darouiche study, the authors ultimately concluded that for every increase of 10 CFUs/m^3 there was a doubling of the risk of PJI.[7] As the number of particles increases over the surgical site, the infection risk increases. When these particles (and thus bacteria) are removed from the air over the surgical site, the deep (but not superficial) SSIs are prevented.

Given Dr. Elghobashi's CFD test, along with the results of the Stocks and Darouiche studies, use of the Bair Hugger during Mrs. Trombley's surgery is the most likely cause of the bacteria inoculating the joint and thus the cause of PJI in this case.

b. The McGovern Study

As previously stated in my general causation expert report, the McGovern study reports a relative risk ratio (odd ratio) of 3.8 comparing use of Bair Hugger to conductive blankets in arthroplasty surgeries. However, relying on a draft data set, Defendants' experts assert that the odds ratio is 2.8 rather than 3.8. Whether one uses the published data in the McGovern study or the draft data used by Dr. Holford, the evidence shows more than a doubling of the risk (RR of $\geq$ 2.0) when Bair Hugger is used compared to non-forced air warming devices such as conductive blankets. The risk ratio reported by McGovern et al. further shows that Bair Hugger is the most likely cause of bacteria inoculating the implant.[8] Under normal OR and surgical procedures, the most likely cause of Mrs. Trombley's PJI was thus the Bair Hugger.

IV. RISK ASSOCIATED WITH MEDICAL DEVICES THAT DISRUPT UNIDIRECTIONAL OR LAMINAR FLOW OPERATING ROOM AIR.

As mentioned above, the CFD studies demonstrate that when the Bair Hugger is set to warm in the OR that it disrupts the air circulation–even in ORs with unidirectional or laminar airflow. This leads to increased particles, many of which

[7] *See* Jarvis General Causation Expert Report at 24 (*citing* Stocks and Darouiche).
[8] *See, e.g.*, Holford Dep. at 225:19-226:1.

carry bacteria, above and in the operative field. Recent infections traced to heater-cooler devices (HCDs) used with patients undergoing cardiopulmonary bypass (CPB) illustrate how such air disruption can occur unrecognized for many years or decades. HCDs have been marketed in the United States since the 1990s. Before 2015, no SSIs had been traced to these devices. However, after two patients were reported with an unusual pathogen, *Mycobacterium chimeara*, causing SSI after cardiac surgery, clinicians began evaluating the potential cause of these infection[9]. Swiss investigators traced the infections to the Sorin/LivaNova 3T HCDs used in the OR[10-17]. These devices are placed much farther away from the operative field and have no patient contact, unlike Bair Huggers. Yet, they were found to release contaminated air from the device and these particles circulated over long distances and contaminated the patients' open surgical wound and caused serious and even deadly SSIs. Subsequently, investigators from a wide variety of countries around the world found similar infections caused by *M. chimaera* and other non-tuberculous mycobacteria and Gram-negative organisms that previously had not been recognized [10-17]. It should be noted that the attack rate with these HCDs has been estimated at 0.25 per million population or 0.94 per 1,000 valve replacement surgeries. Thus, these are low frequency events and account for a small proportion of SSIs/infections

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[9] Achermann Y, Rössle M, Hoffmann M, Deggim V, Kuster S, Zimmermann DR, Bloemberg G, Hombach M, Hasse B. Prosthetic valve endocarditis and bloodstream infection due to *Mycobacterium chimaera*. J Clin Microbiol. 2013;51:1769-73.

[10] https://www.fda.gov/medicaldevices/productsandmedicalprocedures/cardiovasculardevices/heater-coolerdevices/ucm492590.htm

[11] https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm610394.htm

[12] https://www.fda.gov/download/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM505732.pdf

[13] van Ingen J, Kohl TA, Kranzer K, Hasse B, Keller PM, Katarzyna Szafrańska A, et al. Global outbreak of severe *Mycobacterium chimaera* disease after cardiac surgery: a molecular epidemiological study. Lancet Infect Dis. 2017;17:1033–41.

[14] Sommerstein R, Schreiber PW, Diekema DJ, Edmond MB, Hasse B, Marschall J, et al. *Mycobacterium chimaera* outbreak associated with heater-cooler devices: piecing the puzzle together. Infect Control Hosp Epidemiol. 2017;38:103–8.

[15] Kohler P, Kuster SP, Bloemberg G, Schulthess B, Frank M, Tanner FC, et al. Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections subsequent to open heart surgery. Eur Heart J. 2015;36:2745–53.

[16] Schreiber PW, Kuster SP, Hasse B, Bayard C, Rüegg C, Kohler P, et al. Reemergence of *Mycobacterium chimaera* in heater-cooler units despite intensified cleaning and disinfection protocol. Emerg Infect Dis. 2016;22:1830–3.

[17] Allen KB, Yuh DD, Schwartz SB, Lange RA, Hopkins R, Bauer K, et al. Nontuberculous Mycobacterium Infections Associated With Heater-Cooler Devices. Ann Thorac Surg. 2017;104:1237-1242.

[18] Sommerstein R, Hasse B, Marschall J, Sax H, Genoni M, Schlegel M, et al. Global Health Estimate of Invasive *Mycobacterium chimaera* Infections Associated with Heater–Cooler Devices in Cardiac Surgery. Emerg Infect Dis 2018;22:1830-1833.

after cardiac surgery. Yet, despite this, worldwide it is estimated that 156-282 cases/yr occur in the 10 major cardiac valve replacement market countries and 51-80 cases have occurred in the United States alone. The case-fatality rate has been approximately 50%. So, despite the low frequency of occurrence, major morbidity and mortality has occurred with these HCD-related infections.

In light of the research on HCDs, the CDC has recommended that medical devices that disrupt air in the OR be removed from the OR. Thus, a hazardous medical device can be used for decades in the OR and if it is associated with a low rate of infection, especially if caused by usual common skin pathogens, it may not be recognized as a serious risk[8-19]. The Food and Drug Administration (FDA) had approved HCDs for use in the United States and was totally unaware of their infectious risk. Before the HCD outbreaks, it was the opinion of the FDA that HCDs were safe and did not pose a risk to patients. The FDA turned out to be wrong.

As illustrated by the depositions of Drs. Beer, Abdul-Aziz and CRNA Peterson, most clinicians know very little about the design or potential hazards associated with the Bair Hugger or the published literature, much less 3M unpublished data/studies, showing that the Bair Hugger increases particles over the operative field and those particles can carry bacteria that will lead to SSIs. Even the Proceedings of the International Consensus Meeting on Periprosthetic Joint Infections states the particles over the operative field carry bacteria and increase the risk of SSI[19]. Furthermore, the International Consensus states that data show Forced Air Warmers increase particle counts over the operative field. These and other data (including unpublished communications from 3M) document that the Bair Hugger increases particle counts over the operative field, that these particles can carry bacteria, and that this increases the concern and risk for PJIs.

V. GROUP B STREPTOCOCCUS AS A CAUSE OF PROSTHETIC JOINT INFECTIONS (PJIs)

Group B Streptococcus (GBS) is a Gram-positive bacteria. GBS is most commonly seen as a cause of vaginal colonization (not infection) in pregnant females and in invasive infection in their neonates through direct contact during delivery. In one study, GBS-colonization was detected in 5% of feces in older females[20]. Studies of GBS osteoarthritic infections have found that usually they

[19] Kuehl R, Banderet F, Egli A, Keller PM, Frei R, Döbele T, et al. Different Types of Heater-Cooler Units and Their Risk of Transmission of *Mycobacterium chimaera* During Open-Heart Surgery: Clues From Device Design. Infect Control Hosp Epidemiol. 2018;39:834-840.

[20] Islam AK and Thomas E. Faecal carriage of group B streptococci. J Clin Pathol. 1980;33:1006-8.

are secondary to a GBS infection at another site, such as skin, pneumonia, urinary tract, or blood, and occur long after the prosthetic implant. In one large study, such osteoarthritic infections were much more common in men than women and the median time between orthopedic device implantation and onset of Streptococcal infection was 447 days[21]. In a comprehensive study of elective hip and knee arthroplasty infections in the United Kingdom, GBS accounted for less than 8% of the infection nationwide[22]. Thus, PJIs are rarely caused by GBS and, when they occur, they are associated with a preceding infection at another site, and presentation long after the implant procedure.

VI. Additional Recent Relevant Publications

A. Jeans E, Holleyman R, Tate D, Reed M, Malviya A. Methicillin sensitive *Staphylococcus aureus* screening and decolonization in elective hip and knee arthroplasty. J Infect. 2018;77:405-409.

This paper evaluated in a before/after study the impact of screening for Methicillin-susceptible *Staphylococcus aureus* (MSSA) and decolonizing with octenisan bathing for 5 days before surgery and intra-nasal bactroban for 5 days before and after the surgery on THA or TKA SSIs (both superficial and deep). There are several important issues with this paper. First, it is a before/after study not a randomized controlled trial. Second, octenisan has not been a widely used or successful agent for decolonizing MSSA (chlorhexidine has been). Third, the rate of total knee arthroplasty MSSA-SSIs did not significantly decrease. Fourth, the rate of non-MSSA TKA SSIs actually increased. (Mrs. Trombley's PJI was caused by GBS and not MSSA and there are no data to suggest that such a screening and decolonization strategy would have impacted her risk of GBS, rendering any tangential relevance of this study essentially nonexistent in this case.). Fifth, the authors conclude: "the knee replacement cohort did not have a proportionate benefit from the screening program with no change in overall infection rate or MSSA infection rate." Sixth, there was no stratification of the data by superficial or deep SSIs. Given that the mechanism of infection may be different, such an analysis should have been done. Seventh, even if one were to argue that such an intervention would impact THA and TKA MSSA-SSIs, it should be noted that in both groups in the intervention period such MSSA-SSIs still

[21] Seng P, Vernier M, Gay A, Pinelli PO, Legré R, Stein A. Clinical features and outcome of bone and joint infections with streptococcal involvement: 5-year experience of interregional reference centres in the south of France. New Microbes New Infect. 2016;12:8-17.

[22] Hickson CJ, Metcalfe D, Elgohari S, Oswald T, Masters JP, Rymaszewska M, Reed MR, Sprowson AP. Prophylactic antibiotics in elective hip and knee arthroplasty: an analysis of organisms reported to cause infections and National survey of clinical practice. Bone Joint Res. 2015;4:181-9.

occurred—they were ***not*** eradicated by such treatment. In fact, Dr. Reed and colleagues admit that "improvement in infection rates could have been [due] to other factors than MSSA screening."

B. Jain S and Reed M. Laminar air flow handling systems in the operating room. Surgical Infection 2019;20:1-8.

This paper is a review of the current evidence for and against the use of laminar air flow (LAF) systems in ORs. The authors note that "airborne particles carrying contaminating microorganisms are responsible for 98% of surgical site infections." Furthermore, they indicate that the "main problem with LAF is turbulence caused by physical barriers and heat sources obstructing and diverting contaminated air flow currents toward the incision." Last, they point out that "forced air warmers could be considered detrimental to effective laminar air flow and this has been recognized by the National Institute for Health and Care Evidence guidelines on peri-operative warming in orthopedic surgery" and that the authors recommended "a resistive heating mattress or blanket instead of a forced air warmer device."

C. Parvizi J, Barnes S, Shohat N and Edmiston CE, JR. Environment of Care: Is it time to reassess microbial contamination of the operating room air as a risk factor for surgical site infection in total joint arthorplasty. Am J Infect Contrl 2017;45:1267-72.

In this review, the authors evaluate the microbial aerosol contamination of the operating environment. They state that "surgical procedures involving an implant are at significant risk after intraoperative contamination from even a minimal microbial inoculum." "Furthermore, there is a general lack of understanding or even misunderstanding of how (and why) airborne microbial populations pose a significant risk to patients undergoing device-implant surgery." "Microbial contamination of air in the OR is an underappreciated factor in the etiology of PJIs and infection after implantation of other selective biomedical devices."

D. Cook TM, Piatt CJ, Barnes S, and Edmiston CE, Jr. The impact of supplemental air disinfection on the outcome of total joint arthorplasty: A pilot analysis.

In this study, the authors compared the SSI rate in total joint (i.e., hip, knee, and shoulder) arthroplasty (TJA) procedures in an OR with high efficiency particulate air (HEPA) filtration and 20 air changes per hour (ACH) with a similar OR with added UV-C air disinfection system used during the procedure. All patients were screened for MSSA and MRSA and if positive decolonized with Bactroban. In addition, the TJA patients had pre-

operative bathing with 4% Chlorhexidine (CHG) and intra-operative irrigation with 0.05% CHG. The only difference between the OR and care of patients in OR-A (with UV-C) and OR-B (without UV-C) was the use of the air UV-C disinfection system. Patient follow-up was at 4 weeks, 3 months and 12 months. In this 15 month study, 496 patients underwent a TJA procedure. There were five PJIs in the control group (all presented within 90 days of the index surgery) and none in the intervention group (1.9% vs 0%, p=0.044). Thus, despite a rigorous skin antisepsis program in both groups, the PJI rate was significantly decreased by the addition of the UV-C air disinfection system.

These authors noted: "Over the last 20 years, several peer-reviewed publications have presented evidence that airborne microbial populations can play a sentinel role in the etiology of SSI, especially in procedures involving implantable biomedical devices, such as prosthetic joints. Surgical procedures involving an implant are at significant risk after intraoperative contamination from even a minimal microbial inoculum (2.0 Log10)." In addition, they stated: "The convective air flow within the OR produces turbulence which can spread airborne particles, posing a potential risk of postoperative infection. These airborne particles including dust, textile fibers, skin scales, and respiratory aerosols may contain viable microorganisms (including S aureus), which are released from the surgical team members and patient into the surrounding air of the OR. These particles have been shown to settle onto surfaces including the surgical wound and instruments."

This study extends and confirms the findings of the Darouiche study mentioned earlier, and illustrates the importance of disinfecting the air coming in contact with the surgical wound and sterile surgical instruments/materials.

VII. CONCLUSION

I have conducted a careful and thorough medical record review allowing me to provide the Court with a causation assessment and/or differential diagnosis and/or differential etiology for Mrs. Trombley's PJI. As part of my methodology and process in this case, I have ruled out all other reasonably likely or probable causes of infection and determined that the Bair Hugger is the most likely cause of Mrs. Trombley's GBS-PJI. In doing so, I have considered all medical evidence made available to me, as outlined herein, and also have reviewed all countervailing possibilities that might be postulated based on Mrs. Trombley's pre-existing medical

conditions as well as the conditions and practices prevailing in the hospital's OR 3 at the time of her right TKA index surgery.

Using this careful, deliberative, well-accepted methodology, comparing Mrs. Trombley's medical history to other infection cases I have seen over my career, and based on my review of all of the medical and scientific papers addressing these issues, as well as my own scientific training, knowledge, and clinical experience, I conclude to a reasonable degree of scientific and medical certainty that Mrs. Trombley developed a GBS-PJI after her index right TKA procedure on December 2, 2011, and that the GBS was inoculated into her operative wound directly or indirectly by the Bair Hugger.

Moreover, based on the available medical records and literature, CFD testing, the expert report of Dr. Samet, the 3.8 odds-ratio reported in the McGovern study and by Dr. Samet, which can be used to demonstrate specific causation, the deposition testimony of Dr. Holford, and other available data discussed in this report and my general causation report, it is my opinion within a reasonable degree of medical probability that use of the Bair Hugger in Mrs. Trombley's right TKA index surgery was the most likely cause of the bacterial exposure that contaminated her right knee prosthesis in this case.

William R. Jarvis, M.D.

Exhibit A-Additional Materials Reviewed

1. Medical records for Mrs. Ada Trombley from:

A. Bay Park Community Hospital oft he ProMedica Health System (11/22/2011-12/4/2011) (Bates # TROMBLEYAL-20BPCH-00001 throughTROMBLEYAL-20BPCH 00276)

B. ProMedica Toledo Hospital (1/11/2012-3/18/2016) (Bates # TROMBLEYAL-47PTH-00089 through TROMBLEYAL-47PTH-00216)

C. Beer Orthopedics records (11/7/2002-2/22/2017) (Bates # TROMBLEYAL-13PPBO-00001 through TROMBLEYAL-13PPBO-00001-00057)

D. Neprology Consultants of Northwest Ohio (Dr. Nina Al-Sabbagh) (5/3/2012-9/17/2012) (Bates # TROMBLEYAL-24NCNWO-00001 though TROMBLEYAL-24NCNWO-0018)

E. Infectious Disease Associates of N.W. Ohio, Inc. (Dr. Nelson Nicolasora) (Bates# TROMBLEYAL-10JVA-00149 through TROMBLEYAL-10JVA-00152)

F. Bay Park Community Hospital Vertical Clean Air System Operating Manual, OR photos, and description.

2. Depositions of CRNA Lauren Peterson, Orthopedic Surgeon Dr. Karl Beer, and Anesthesiologist Dr. Tammam Abdul-Aziz.